REMARKS/ARGUMENTS

Claims 1-3, 5-7, 9-42, 44-53, 56-57 and 203-204 are currently pending in the application. Applicants respectfully submit that the foregoing amendments to the claims are supported in the application as originally filed and that no new matter has been added. In view of the following remarks and amendments, applicants respectfully request a timely Notice of Allowance be issued in this case.

Specification Objections

The two newly added paragraphs [0072.1] and [0072.2] were objected to in the Office Action mailed on January 9, 2008 ("Office Action") as introducing new matter.

With respect to paragraph [0072.1], the phrase "SNIDE providing a method" was objected to as introducing new matter. Applicants respectfully submit that the foregoing amendment changing the phase to "the present invention" is fully supported in the application as filed and does not constitute new matter. Accordingly, applicants respectfully request reconsideration and withdrawal of the objection to paragraph [0072.1].

With respect to paragraph [0072.2], the phrase "modified or reclassified" was objected to as introducing new matter. Applicants respectfully traverse the objection based on paragraphs [0093] and [0095] of the specification where the modification and reclassification of the variation frequency are disclosed (emphasis added):

> [0093] The SNIDE algorithm relies upon aggregate properties of a large mutation dataset, which reflect a likelihood of mutation occurrence and impact, which are used to approximate the local mutational properties of any given gene. It is clear from the data in TABLE 2, however, that the impact portion of the predictiveness number may be **modified**. For example, a Val.fwdarw.Ile mutation may have little or no impact on a protein in most situations, but if it happens to be in a position important for folding or function then the mutation may be causative of some disease. Therefore, the addition of gene-specific factors regarding impact should increase the accuracy of SNIDE. One method for improving accuracy is to analyze conservative versus non-conservative substitutions under the premise that such crucial residues will be conserved roughly proportional to their importance. Homolog searches, 3D structure comparisons, coupling (mutual information), and secondary structure predictions are all components that may be added into SNIDE to modulate predictions based on projected impact.
>
> [0095] **Another way to reclassify** predictions by impact is to consider the effects of the mutation on both DNA and mRNA structure. Such mutations may have negligible effect on the resulting protein structure in the final product but disrupt seriously transcription or translation. One scenario is that a mutation may favor the formation of a thermodynamically stable hairpin in unwound single-stranded DNA that causes the RNA polymerase to skip a chunk of sequence and generate

> a frameshift deletion in the protein. Knowledge of protein structure and amino acid conservation is useful to tailor the mutation predictions even further towards a high impact data set, mRNA and DNA structure may be either predicted (using commercial packages such as MFOLD) or detected experimentally in vitro. FIG. 5 depicts the matrix construction and deployment process when using SNIDE.

Additional examples of adjusting the calculated variation frequency can be found in paragraphs [0065], [0083] and [0085] of the specification. The specification also provides examples ("reclassify" or "modify") in paragraph [0094]. Furthermore, paragraph [0031] states that the words "alteration" and "modification" may be used interchangeably. As a result, applicants respectfully submit that paragraph [0072.2] is fully supported in the application as filed and does not constitute new matter. Accordingly, applicants respectfully request reconsideration and withdrawal of the objection to paragraph [0072.2].

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 5-7, 9-42, 43-53, 56-57, 203 and 204 were rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. More specifically, the elements "one or more groups", "the bases", "will likely occur", "a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset", and "one or more codons" were said to be indefinite. Applicants respectfully request reconsideration and withdrawal of the rejections for the following reasons.

Claims 1, 57 and 203

The element "one or more groups" was amended to recite "one or more bases in the nucleic acid sequence." In addition, the element "the bases" was amended to recite "the one or more bases." Applicants respectfully submit that claims 1, 57 and 203, as amended, particularly point out and distinctly claim the subject matter which applicants regard as the invention and are, therefore, allowable under 35 U.S.C. § 112, second paragraph.. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejections.

In addition, the element "will likely occur" was said to be unclear. Applicants respectfully disagree. The Office Action appears to indicate that the specific transition is identified when in fact the claims recite that the locations are identified. The term "will likely occur" is described in paragraph [0025] (emphasis added):

> [0025] A "variation predictiveness matrix" is defined herein as a table, list or mathematical matrix generated from empirical sequence data that describes the expectation of every possible base to base mutation class to occur in one or more sequences as calculated from that base usage and frequency in a mutation

> database. The variation predictiveness matrix is capable of quantifying and qualifying, independently or concurrently, the likelihood or frequency of a sequence change occurring in a given nucleic acid sequence and/or the likelihood or frequency that the sequence change will have an effect on function, for example, on gene expression, exon expression, translocations, conservative and non-conservative amino acid changes, transcription, translation, termination, secondary, tertiary or quaternary DNA, RNA or protein structure, protein-protein interactions, biochemical activity, cell transport, signal transduction, intra and extracellular messengers, methylation, shuffling, clustering, splicing, message stability, protein stability, post-translational modifications, and the like. The variation predictiveness matrix is generally a list, chart, table or matrix that contains a predictiveness value, .zeta., that may include, e.g., the **likelihood or frequency of a sequence or polymorphism change occurring in a given nucleic acid base** in a sequence and/or the likelihood or frequency that the sequence or polymorphism change will have an effect on function. The predictiveness value may also incorporate other factors that affect the overall score, value or number assigned for the specific matrix. Furthermore, the user of the matrix may change the threshold value of the score assigned to a base using the predictiveness value to increase the accuracy of scan or determination of the likelihood that a change in the sequence, polymorphism or mutation will have an effect at a later stage, e.g., a nonsynonymous change in protein sequence.

Moreover, the specification clearly uses "e.g." in paragraph [0080] to indicate that the mutation from CGA to TGA is only an example. The language used here is not limiting, and a skilled artisan would recognize that other transitions would also be considered. For all the foregoing reasons, applicants respectfully submit that the metes and bounds of the limitations of claim 1 are clear and allowable under 35 U.S.C. § 112, second paragraph. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejections.

Claim 48

The element "a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset" was amended to recite "a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the mutant genes of the mutant gene dataset that are known to cause a disease." This amendment is supported in the paragraph [0062] (emphasis added):

> [0062]…The HGMD is manually curated and only details **mutations that are known to cause a disease**. Because only mutations that are known to cause a disease are in the dataset, the aggregate mutation set is biased towards these "phenogenic" mutations that display a clinically realizable phenotype…

Applicants respectfully submit that claim 48, as amended, particularly points out and distinctly claims the subject matter which applicants regard as the invention and are, therefore, allowable under 35 U.S.C. § 112, second paragraph.. Accordingly, applicants

respectfully request reconsideration and withdrawal of the rejections.

Claim 204

The element "one or more codons" was amended to recite "one or more codons in the wild-type gene sequence." Applicants respectfully submit that claim 204, as amended, particularly points out and distinctly claims the subject matter which applicants regard as the invention and is, therefore, allowable under 35 U.S.C. § 112, second paragraph. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejections.

Claims 2-3, 5-7, 9-42, 44-53 and 56-57

Applicant respectfully submits that claims 2-3, 5-7, 9-42, 44-53 and 56-57 depend from claim 1, as amended, which is allowable for the reasons stated above. Claims 2-3, 5-7, 9-42, 44-53 and 56-57 are, therefore, allowable under 35 U.S.C. § 112, second paragraph. Accordingly, applicant respectfully requests reconsideration and withdrawal of the rejections.

Claim Rejections under 35 U.S.C. § 101

Claims 1-3, 5-7, 9-42, 44-53, 56-57, 203 and 204 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Applicants respectfully request reconsideration and withdrawal of the rejections for the following reasons.

Claim 1

Applicants respectfully submit that claim 1 produces a useful, tangible, and concrete final result because claim 1, as amended, recites a "computer-implemented method" and "outputting the identified locations of the single nucleotide polymorphisms to a computer display, an electronic file or a printer." As disclosed in paragraph [0081] and claim 210 (originally filed), the present invention, among other things, "generat[es] a delimited file suitable for a standard spreadsheet application." Moreover, the use of computer displays, electronic files and printers with computers and computer-implemented methods are common knowledge, well known to those skilled in the art and inherent under MPEP § 2163.07(a). As a result, applicants respectfully submit that claim 1, as amended, is directed to statutory subject matter and is, therefore, allowable under 35 U.S.C. § 101. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejections.

Claims 2-3, 5-7, 9-42, 44-53 and 56-57

Applicant respectfully submits that claims 2-3, 5-7, 9-42, 44-53 and 56-57 depend from claim 1, as amended, which is allowable for the reasons stated above. Claims 2-3,

5-7, 9-42, 44-53 and 56-57 are, therefore, allowable under 35 U.S.C. § 101. Accordingly, applicant respectfully requests reconsideration and withdrawal of the rejections.

Claims 203-204

Applicants respectfully submit that claims 203-204 do not claim a signal because claims 203-204, as amended, recite a "computer readable medium encoded with a computer program." This language has been determined to be statutory pursuant to MPEP § 2106.01(I)(second paragraph). As a result, applicants respectfully submit that claims 203-204, as amended, are directed to statutory subject matter and is, therefore, allowable under 35 U.S.C. § 101. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejections.

Conclusion

Applicants respectfully submit that claims 1-3, 5-7, 9-10, 12, 22, 37-42, 44-53, 56-57 and 203-204, as amended, are fully patentable. Applicants respectfully request that a timely Notice of Allowance be issued in this case. If the examiner has any questions or comments, or if further clarification is required, it is requested that the examiner contact the undersigned at the telephone number listed below.

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Respectfully submitted,

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